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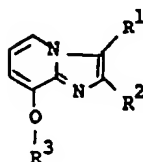
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(54) Imidazopyridine compounds and processes for preparation thereof.

(57) An imidazopyridine compound of the formula:



wherein R¹ is lower alkynyl or lower alkynyloxy-(lower)alkyl,
R² is lower alkyl, and
R³ is ar(lower)alkyl having lower alkoxy, lower alkylthio, ni-
tro or lower alkanesulfonyl, ar(lower)alkyl having nitro and one
or two additional substituent(s) selected from nitro and lower
alkyl, or heterocyclic(lower)alkyl which may have suitable sub-
stituent(s), and a pharmaceutically acceptable salt thereof,
processes for the preparation thereof and pharmaceutical
compositions comprising such compounds in admixture with
pharmaceutically acceptable carriers.

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IMIDAZOPYRIDINE COMPOUNDS AND
PROCESSES FOR PREPARATION THEREOF

The present invention relates to novel imidazopyridine compounds and pharmaceutically acceptable saltsthereof. More particularly, it relates to novel imidazopyridine compounds and pharmaceutically acceptable salts thereof
5 which have antiulcerative activity, to processes for preparation thereof, to pharmaceutical composition comprising the same, and to method of using the same therapeutically in the treatment of ulcer in human being or animals.

10 Accordingly, one object of the present invention is to provide novel imidazopyridine compounds and pharmaceutically acceptable salt thereof, which are useful as a medicine for ulcer.

15 Another object of the present invention is to provide processes for preparation of said imidazopyridine compounds and pharmaceutically acceptable saltsthereof.

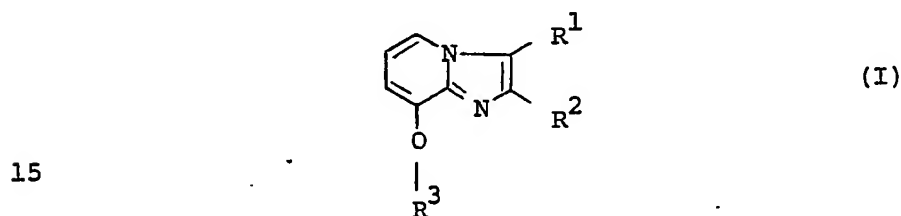
A further object of the present invention is to provide pharmaceutical composition comprising,

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as an active ingredient, said imidazopyridine compound or its pharmaceutically acceptable salt.

Still further object of the present invention is to provide method of using said imidazopyridine compound or its pharmaceutically acceptable salt in the treatment of ulcer in human being or animals.

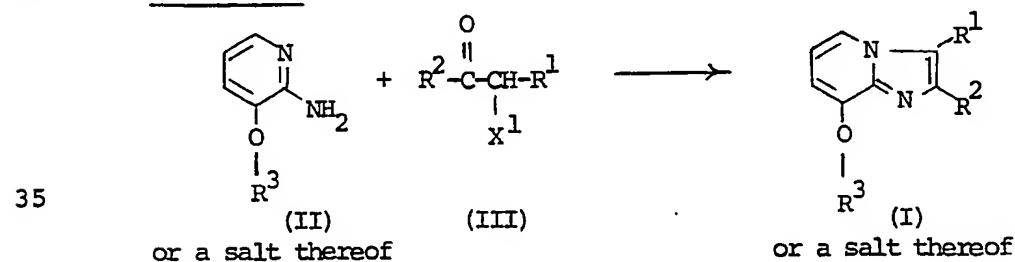
The imidazopyridine compounds of the present invention are novel and can be represented by the formula (I) :



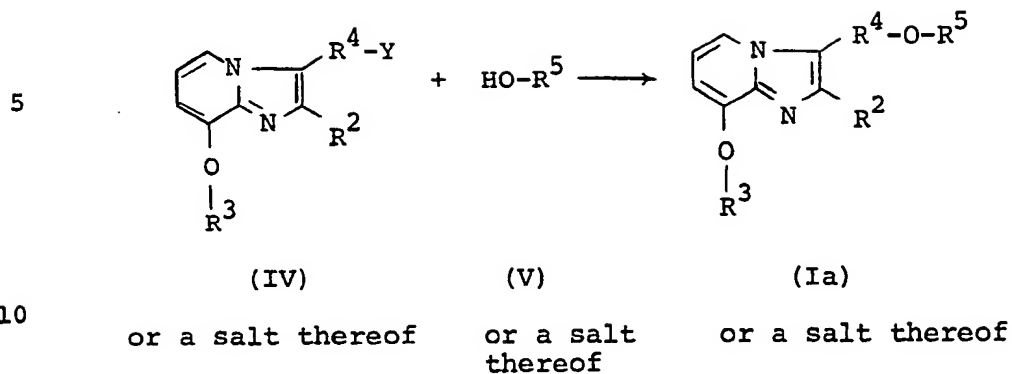
wherein R^1 is lower alkynyl or lower alkynyloxy(lower)-alkyl,
 R^2 is lower alkyl, and
 R^3 is ar(lower)alkyl having lower alkoxy, lower alkylthio, nitro or lower alkanesulfonyl, ar(lower)alkyl having nitro and one or two additional substituent(s) selected from nitro and lower alkyl, or heterocyclic-(lower)alkyl which may have suitable substituent(s).

According to the present invention, the object compound (I) can be prepared by the following processes.

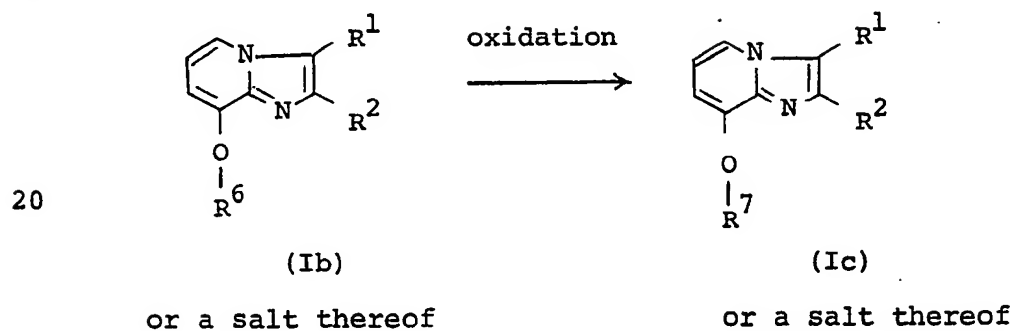
Process 1



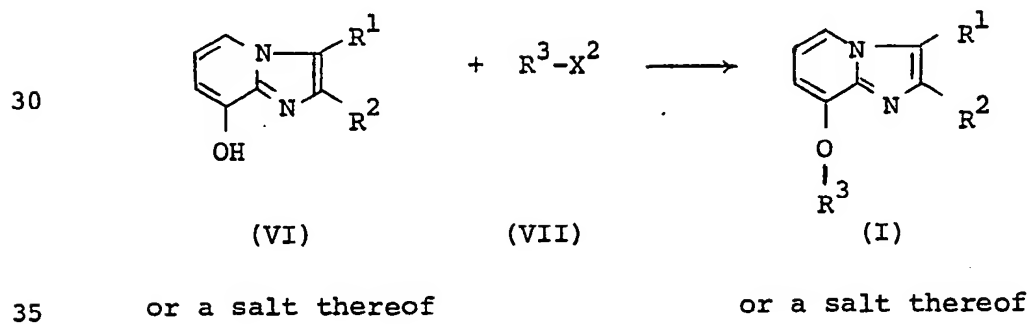
Process 2



Process 3



Process 4



wherein R^1 , R^2 and R^3 are each as defined above,
 R^4 is lower alkylene,
 R^5 is lower alkynyl,
 R^6 is ar(lower)alkyl which has lower alkylthio,
 R^7 is ar(lower)alkyl which has lower
 alkanesulfonyl,
 X^1 and X^2 are each an acid residue, and
 Y is a leaving group.

As to the starting compounds (II), (III), (IV) and (VI), some of them are novel and can be prepared by the procedures disclosed in the following Preparations 1 to 19.

Suitable pharmaceutically acceptable salts of the object compounds (I) are conventional non-toxic salts and include an organic acid salt (e.g. acetate, maleate, tartrate, methanesulfonate, benzenesulfonate, formate, toluenesulfonate, etc.), an inorganic acid salt (e.g. hydrochloride, hydrobromide, sulfate, phosphate, etc.), a salt with an amino acid (e.g., arginine, aspartic acid, glutamic acid, etc.), and the like.

In the above and subsequent descriptions of the present specification, suitable examples and illustrations of the various definitions which the present invention include within the scope thereof are explained in detail as follows.

The term "lower" is intended to mean 1 to 6 carbon atom(s), unless otherwise indicated.

Suitable "lower alkynyl" and suitable "lower alkynyl moiety" in the term "lower alkynyloxy(lower)-alkyl" may be the ones having 2 to 6 carbon atoms and may include ethynyl, 1(or 2)-propynyl, 1(or 2 or 3)-butynyl, 1(or 2 or 3 or 4)-pentynyl, 1(or 2 or 3 or 4 or 5)-hexynyl and the like.

Suitable "lower alkyl" and suitable "lower alkyl moiety" in the terms "lower alkynyloxy(lower)alkyl" and "heterocyclic(lower)alkyl" may be the ones having 1 to 6 carbon atom(s) and may include methyl, ethyl, propyl, isopropyl, n-butyl, t-butyl, pentyl, hexyl and the like.

Suitable "ar(lower)alkyl" may include mono(or di or tri)-phenyl(lower)alkyl such as benzyl, benzhydryl, trityl, phenethyl or the like.

Suitable "heterocyclic moiety" in the term "heterocyclic(lower)alkyl" may be 3 to 7 membered (more preferably 5 or 6 membered) heteromonocyclic group having 1 to 3 hetero atom(s) such as thienyl, furyl, pyrrolyl, pyrazolyl, thiazolyl, thiadiazolyl, triazolyl, pyridyl, pyridazinyl, triazinyl or the like.

Said "heterocyclic(lower)alkyl" may have one or more, preferably one to three suitable substituent(s) such as lower alkyl (e.g. methyl, ethyl, propyl, n-butyl, t-butyl, pentyl, hexyl, etc.), lower alkoxy (e.g. methoxy, ethoxy, propoxy, butoxy, t-butoxy, pentyloxy, hexyloxy, etc.), acylamino such as lower alkanamido (e.g. formamido, acetamido, etc.) or the like.

Suitable "lower alkylene" may include methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene and the like.

Suitable "an acid residue" may include halogen (e.g. fluorine, chlorine, bromine, iodine), acyloxy (e.g. acetoxy, tosyloxy, mesyloxy, etc.) and the like.

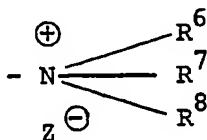
Suitable "lower alkoxy" may include methoxy, ethoxy, propoxy, butoxy, t-butoxy, pentyloxy, hexyloxy and the like.

Suitable "lower alkylthio" may include methylthio, ethylthio, propylthio, butylthio, t-butylthio, pentylthio, hexylthio and the like.

Suitable "lower alkanesulfonyl" may include mesyl,

ethanesulfonyl, propanesulfonyl, butanesulfonyl, t-butesulfonyl, pentanesulfonyl, hexanesulfonyl and the like.

5 Suitable "a leaving group" may include an acid residue as mentioned above, a group of the formula :



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wherein R^6 , R^7 and R^8 are each lower alkyl as mentioned above, and

Z is an acid residue as mentioned above, and the like.

15

Preferred embodiments of the object compounds (I) are as follows.

Preferred embodiment of R^1 is lower alkynyl, more preferably $\text{C}_2\text{-C}_3$ alkynyl; or lower alkynyloxy(lower)alkyl, more preferably $\text{C}_2\text{-C}_3$ alkynyloxy($\text{C}_1\text{-C}_3$)alkyl.

20

Preferred embodiment of R^2 is lower alkyl, more preferably $\text{C}_1\text{-C}_3$ alkyl.

25

Preferred embodiment of R^3 is phenyl(lower)alkyl having lower alkoxy, more preferably phenyl($\text{C}_1\text{-C}_3$)alkyl having ($\text{C}_1\text{-C}_3$)alkoxy; phenyl(lower)alkyl having lower alkylthio, more preferably phenyl($\text{C}_1\text{-C}_3$)alkyl having ($\text{C}_1\text{-C}_3$)alkylthio; phenyl(lower)alkyl having nitro, more preferably phenyl($\text{C}_1\text{-C}_3$)alkyl having nitro; phenyl(lower)alkyl having lower alkanesulfonyl, more preferably phenyl($\text{C}_1\text{-C}_3$)alkyl having ($\text{C}_1\text{-C}_3$)alkanesulfonyl; 3 to 7 membered heteromonocyclic(lower)alkyl which may have lower alkyl, more preferably 5 or 6 membered heteromonocyclic($\text{C}_1\text{-C}_3$)alkyl which may have ($\text{C}_1\text{-C}_3$)alkyl; 3 to 7 membered heteromonocyclic(lower)alkyl which may have lower alkoxy, more preferably 5 or 6 membered

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heteromonocyclic(C₁-C₃)alkyl which may have (C₁-C₃)alkoxy;
 3 to 7 membered heteromonocyclic(lower)alkyl which may
 have acylamino, more preferably 5 or 6 membered
 heteromonocyclic(C₁-C₃)alkyl which may have (C₁-C₃)-
 5 alkanoylamino; phenyl(lower)alkyl having nitro and
 lower alkyl, more preferably phenyl(C₁-C₃)alkyl having
 nitro and (C₁-C₃)alkyl; or phenyl(lower)alkyl having
 nitro and two lower alkyl, more preferably phenyl-
 10 (C₁-C₃)alkyl having nitro and two (C₁-C₃)alkyl.

The processes for preparing the object compounds
 of the present invention are explained in detail in
 the following.

15 Process 1

The object compound (I) or a salt thereof can be
 prepared by reacting the compound (II) or a salt
 thereof with the compound (III).

20 Suitable salts of the compound (II) can be referred
 to the acid addition salt as exemplified for the compound
 (I).

This reaction is usually carried out in a solvent
 such as alcohol [e.g. methanol, ethanol, etc.],
 benzene, N,N-dimethylformamide, tetrahydrofuran,
 25 diethyl ether or any other solvent which does not
 adversely affect the reaction.

The reaction may be carried out in the presence
 of an inorganic or an organic base such as an alkali
 metal hydroxide [e.g. sodium hydroxide, potassium
 30 hydroxide, etc.], an alkali metal carbonate [e.g.
 sodium carbonate, potassium carbonate, etc.], an
 alkali metal bicarbonate [e.g. sodium bicarbonate,
 potassium bicarbonate, etc.], tri(lower)alkylamine
 [e.g. trimethylamine, triethylamine, etc.], pyridine
 35 or its derivative [e.g. picoline, lutidine,

4-dimethylaminopyridine, etc.], or the like. In case that the base to be used is liquid, it can also be used as a solvent.

5 The reaction temperature is not critical, and the reaction can be carried out under cooling, at ambient temperature or under warming or heating.

Process 2

10 The object compound (Ia) or a salt thereof can be prepared by reacting the compound (IV) or a salt thereof with the compound (V) or a salt thereof.

Suitable salts of the compounds (IV) and (Ia) can be referred to the ones as exemplified for the object compound (I).

15 Suitable salts of the compound (V) are salts with a base such as an alkali metal salt (e.g. sodium salt, potassium salt, lithium salt, etc.) or the like.

This reaction is usually carried out in the presence of a base such as alkali metal hydride (e.g. sodium hydride, potassium hydride, lithium hydride, etc.), alkali metal alkoxide (e.g. potassium t-butoxide, etc.), an alkali metal (e.g. sodium, potassium, lithium, etc.) or the like.

25 This reaction is usually carried out in a solvent such as alcohol [e.g. methanol, ethanol, etc.], dimethyl sulfoxide, benzene, N,N-dimethylformamide, tetrahydrofuran, diethyl ether or any other solvent which does not adversely affect the reaction.

In case that the compound (V) or a salt thereof to be used is liquid, it can also be used as a solvent.

30 The reaction temperature is not critical, and the reaction can be carried out under cooling, at ambient temperature or under warming or heating.

35

Process 3

The object compound (Ic) or a salt thereof can be prepared by subjecting the compound (Ib) or a salt thereof to oxidation reaction.

5 Suitable salts of the compounds (Ib) and (Ic) can be referred to the ones as exemplified for the object compound (I).

10 Suitable example of oxidizing agent to be used in this reaction may include all oxidizing agents, which can oxidize -S- group to -SO₂- group and do not adversely affect the compounds (Ib) or (Ic), for example, peroxy-acid such as hydrogen peroxide, perbenzoic acid, perphthalic acid, performic acid, peracetic acid, trifluoroperacetic acid,
15 m-chloroperbenzoic acid or the like.

20 This reaction is usually carried out in a solvent such as acetic acid, chloroform, methylene chloride, diethyl ether, dioxane, benzene or any other solvent which does not adversely affect the reaction.

25 The reaction temperature is not critical and the reaction is usually carried out under cooling, at ambient temperature, under warming or heating.

25 Process 4

 The object compound (I) or a salt thereof can be prepared by reacting the compound (VI) or a salt thereof with the compound (VII).

30 Suitable salts of the compound (VI) can be referred to the salt as exemplified for the compound (I).

 This reaction is usually carried out in a solvent such as alcohol [e.g. methanol, ethanol, etc.], benzene, N,N-dimethylformamide, tetrahydrofuran, diethyl ether or any other solvent which does not
35 adversely affect the reaction.

The reaction may be carried out in the presence of an inorganic or an organic base such as an alkali metal hydroxide [e.g. sodium hydroxide, potassium hydroxide, etc.], an alkali metal carbonate [e.g. sodium carbonate, potassium carbonate, etc.], an alkali metal bicarbonate [e.g. sodium bicarbonate, potassium bicarbonate, etc.], tri(lower)alkylamine [e.g. trimethylamine, triethylamine, etc.], pyridine or its derivative [e.g. picoline, lutidine, 4-dimethylaminopyridine, etc.], or the like. In case that the base to be used is liquid, it can also be used as a solvent.

The reaction temperature is not critical, and the reaction can be carried out under cooling, at ambient temperature or under warming or heating.

The object compounds (I) and their pharmaceutically acceptable salts of the present invention are novel and exhibit high inhibitory activity on ulcer.

In order to illustrate the usefulness of the object compound (I), the pharmacological data of the representative compound of the object compounds (I) are shown in the following.

(A) Inhibition on ethanol ulcer

25 Test Method :

Five male Sprague-Dawley rats, aged 7 weeks and weighing about 200 g, were used per group for the study on ethanol ulcer after the fast for 24 hours.

30 Test compound was suspended in 0.1% methylcellulose aqueous solution, and the suspension (5 ml/kg) was orally given to each rat.

The control group was given a vehicle, i.e. 0.1% methylcellulose aqueous solution (5 ml/kg), alone in the same way.

35 Absolute ethanol (5 ml/kg) was orally administered

30 minutes after dosing with test compound, and one hour later, the rats were sacrificed and their stomachs were removed. The area of ulcers of each rat was measured. The mean area (mm) in the medicated group was compared with that in the control group.

Test Compounds

(1) 8-(2-Methoxybenzyloxy)-2-methyl-3-(2-propynyloxy-methyl)imidazo[1,2-a]pyridine

Test Result

Inhibition % at the dose of 32 mg/kg :

Test Compound	Inhibition %
(1)	95.7

(B) Inhibition on stress ulcer

Test Method :

Five Sprague-Dawley rats weighing about 200 g were used per group. Each animal was immobilized in a small cage and put in a water bath allowing to respire. The temperature of the water bath kept as 22°C. The test compound was administered orally just before the immobilization. Seven hours later, the animals were sacrificed and their stomachs were removed. The stomach was then fixed with 2% formalin. The area of ulcers was measured for each animal. The mean area (mm²) in the medicated animals was compared with that in the control animals.

Test Compounds

(1) 8-(2-Methoxybenzyloxy)-2-methyl-3-(2-propynyl)-imidazo[1,2-a]pyridine

Test Result

Inhibition % at the dose of 32 mg/kg :

Test Compound	Inhibition %
(1)	100

5

10 As being apparent from the above test results,
the object compound (I) of the present invention are
useful as antiulcer medicines.

15 For therapeutic purpose, the compounds according
to the present invention can be used in a form of
pharmaceutical preparation containing said compound
as an active ingredient, in admixture with a pharma-
ceutically acceptable carrier such as an organic or
inorganic solid or liquid excipient suitable for oral
or parenteral administration. The pharmaceutical
20 preparations may be capsules, tablets, dragees, solution,
suspension, emulsion, and the like. If desired,
there may be included in the above preparations
auxiliary substances, stabilizing agents, wetting or
emulsifying agents, buffers and other commonly used
25 additives.

While the dosage of the compounds will vary
depending upon the age and condition of the patient,
an average single dose of about 5 mg, 10 mg, 50 mg,
100 mg, 250 mg, 500 mg, and 1000 mg of the compounds
30 according to the present invention may be effective
for treating ulcer. In general, amounts between
1 mg/body and about 2,000 mg/body or even more may
be administered per day.

35 The following preparations and examples are given
for the purpose of illustrating the present invention.

Preparation 1

Tosyl chloride (3.81 g) was added to a solution of 3-hydroxy-5-hexyn-2-one (2.24 g) and triethylamine (2.424 g) in methylene chloride (20 ml) under ice-cooling. After being stirred for 2.5 hours, the mixture was washed with water, dried over magnesium sulfate and evaporated in vacuo. The oily residue was purified by column chromatography on silica gel (60 g) using methylene chloride as an eluent to give an oil of 3-tosyloxy-5-hexyn-2-one (2.94 g).

IR (film/NaCl) : 3280, 1720, 1590, 1360 (broad) cm^{-1}

NMR (CCl_4 , δ) : 1.79 (1H, t, $J=2\text{Hz}$), 2.25 (3H, s), 2.43 (3H, s), 2.3-2.6 (2H, m), 4.66 (1H, t, $J=5\text{Hz}$), 7.31 (2H, d, $J=8\text{Hz}$), 7.78 (2H, d, $J=8\text{Hz}$)

Preparation 2

To a mixture of 2-amino-3-hydroxypyridine (7.64 g) and Adogen 464 (Trademark: prepared by Aldrich Chemical Co.) (0.42 g) in 40% aqueous sodium hydroxide (35 ml) and methylene chloride (35 ml) was added 2-methoxybenzyl chloride (10.87 g) at ambient temperature. After being stirred for 22 hours, the organic layer was separated and the aqueous layer was extracted with methylene chloride. The combined extracts were washed with saturated sodium chloride aqueous solution, dried over magnesium sulfate, and evaporated in vacuo. The crystalline residue was recrystallized from ethyl acetate to give 2-amino-3-(2-methoxybenzyloxy)pyridine (6.09 g).

mp : 111 to 113°C (recrystallized from a mixture of methylene chloride and diisopropyl ether)

IR (Nujol) : 3430, 3205, 3180, 1627 cm^{-1}

NMR (CDCl_3 , δ) : 3.81 (3H, s), 4.82 (2H, broad s),

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5.08 (2H, s), 6.52 (1H, dd, J=4Hz and 7Hz),
6.80-7.09 (3H, m), 7.17-7.46 (2H, m),
7.62 (1H, d, J=4Hz)

5 Preparation 3

The following compounds were prepared according
to a similar manner to that of Preparation 2.

- 10 (1) 2-Amino-3-(2-methylthiobenzoyloxy)pyridine
mp : 101 to 103°C (recrystallized from a mixture
of ethyl acetate and n-hexane)
IR (Nujol) : 3450, 3270, 3145, 1620 cm^{-1}
NMR (CDCl_3 , δ) : 2.47 (3H, s), 4.78 (2H, broad s),
5.12 (2H, s), 6.44-6.68 (1H, m),
15 6.99 (1H, d, J=7Hz), 7.11-7.50 (4H, m),
7.67 (1H, dd, J=2Hz and 5Hz)
- 20 (2) 2-Amino-3-(2-nitrobenzoyloxy)pyridine
mp : 139 to 141°C (recrystallized from chloroform)
IR (Nujol) : 3450, 3260, 3100, 1625, 1520, 1350 cm^{-1}
NMR ($\text{DMSO}-d_6$, δ) : 5.50 (2H, s), 5.73 (2H, broad s),
6.40-6.66 (1H, m), 7.12 (1H, dd, J=2Hz and
10Hz), 7.46-8.30 (5H, m)

25 Preparation 4

To a solution of 2-amino-3'-hydroxypyridine
(15.18 g) in N,N-dimethylformamide (150 ml) was added
portionwise a 60% dispersion of sodium hydride in
mineral oil (6.06 g) with ice-cooling and stirring
30 over a period of 10 minutes. After being stirred at
0-5°C for 30 minutes and then at ambient temperature
for 1 hour, a solution of 2-chloromethyl-3-
methylthiophene (23.9 g) in N,N-dimethylformamide
(10 ml) was added dropwise to the reaction mixture.
35 The mixture was stirred at ambient temperature for 20

hours and poured into water. The resulting precipitate was collected by filtration and dissolved in methylene chloride. The solution was treated with activated charcoal and evaporated in vacuo. The residue was
5 crystallized from diethyl ether to give 2-amino-3-(3-methyl-2-thienylmethoxy)pyridine (23.6 g).

mp : 131 to 132.5°C

IR (Nujol) : 3480, 3280, 3100, 1625 cm^{-1}

10 NMR (DMSO-d_6 , δ) : 2.25 (3H, s), 5.18 (2H, s),
5.52 (2H, broad s), 6.36-6.66 (1H, m),
6.89 (1H, d, $J=5\text{Hz}$), 7.13 (1H, dd, $J=1\text{Hz}$
and 8Hz), 7.41 (1H, d, $J=5\text{Hz}$), 7.54 (1H, dd,
 $J=2\text{Hz}$ and 5Hz)

15 Preparation 5

A 60% dispersion of sodium hydride in mineral oil (0.3 g) was added portionwise to a suspension of 8-hydroxy-2-methylimidazo[1,2-a]pyridine (1.0 g) in dimethyl sulfoxide (10 ml) at room temperature over a
20 period of 15 minutes. After being stirred for 30 minutes, 4-nitrobenzyl bromide (1.6 g) was added in one portion to the mixture and then the resultant mixture was stirred for 24 hours at room temperature. The mixture was poured into water and the resulting
25 precipitate was collected by filtration. The crude product was purified by column chromatography on silica gel (30 g) with methylene chloride as an eluent to afford a solid, which was recrystallized from a mixture of ethyl acetate and n-hexane to give 2-methyl-8-(4-nitrobenzyloxy)imidazo[1,2-a]pyridine (0.77 g).
30

mp : 160 to 165°C

NMR (CDCl_3 , δ) : 2.50 (3H, s), 5.40 (2H, s),
6.20-6.70 (2H, m), 7.33 (1H, s), 7.46-7.80
(3H, m), 8.16 (2H, d, $J=8\text{Hz}$)

Preparation 6

The following compounds were prepared according to a similar manner to that of Preparation 5.

- 5 (1) 8-(2-Methoxybenzyloxy)-2-methylimidazo[1,2-a]pyridine
NMR (CDCl₃, δ) : 2.46 (3H, s), 3.85 (3H, s),
5.36 (2H, s), 6.23-6.66 (2H, m), 6.72-7.06
(2H, m), 7.10-7.36 (2H, m), 7.37-7.70 (2H, m)
- 10 (2) 2-Methyl-8-(2-nitrobenzyloxy)imidazo[1,2-a]pyridine
mp : 158 to 160°C (recrystallized from ethanol)
NMR (CDCl₃, δ) : 2.49 (3H, s), 5.73 (2H, s),
6.26-6.76 (2H, m), 7.25-7.83 (4H, m), 7.96
(1H, s), 8.15 (1H, dd, J=2Hz, 8Hz)

15

Preparation 7

To a solution of 37% aqueous formaldehyde (1.57 g) in acetic acid (25 ml) was added dropwise 50% aqueous dimethylamine (1.75 g) with ice-cooling over a period
20 of 10 minutes and the mixture was stirred for an additional 10 minutes. The mixture was heated at 50-55°C for 2 hours after an addition of 8-(2-methoxybenzyloxy)-2-methylimidazo[1,2-a]pyridine (4.96 g) thereto and then evaporated in vacuo. The residue was basified with
25 aqueous sodium hydroxide and extracted with methylene chloride. The extract was washed with water, dried over magnesium sulfate and evaporated in vacuo. The residual solid was recrystallized from diethyl ether to give 3-dimethylaminomethyl-8-(2-methoxybenzyloxy)-2-methylimidazo[1,2-a]pyridine (3.55 g).

30

mp : 139 to 141°C

NMR (CDCl₃, δ) : 2.20 (6H, s), 2.43 (3H, s),
3.58 (2H, s), 3.83 (3H, s), 5.33 (2H, s),
6.35-6.69 (6H, m), 6.89 (2H, t, J=5Hz),
7.13-7.36 (1H, m), 7.52 (1H, b.d, J=5Hz),
35 7.76 (1H, dd, J=1Hz, 4Hz)

Preparation 8

The following compound was prepared according to a similar manner to that of Preparation 7.

5 3-Dimethylaminomethyl-2-methyl-8-(2-nitrobenzyloxy)-imidazo[1,2-a]pyridine

mp : 160 to 162°C

10 NMR (CDCl₃, δ) : 2.20 (6H, s), 2.46 (3H, s),
3.60 (2H, s), 5.72 (2H, s), 6.30-6.80
(2H, m), 7.23-8.06 (4H, m), 8.16 (1H, dd,
J=2Hz, 7Hz)

Preparation 9

15 Methyl iodide (1.08 g) was added dropwise to a solution of 3-dimethylaminomethyl-8-(2-methoxybenzyloxy)-2-methylimidazo[1,2-a]pyridine (3.42 g) in acetone (34 ml) and chloroform (10 ml) at room temperature and the mixture was stirred for 24 hours. The resulting precipitate was collected by filtration, washed with acetone, and dried in a desiccator to give 8-(2-methoxybenzyloxy)-2-methyl-3-trimethylammoniomethyl-imidazo[1,2-a]pyridine iodide (3.63 g).

mp : >160°C (dec.)

25 NMR (DMSO-d₆, δ) : 2.49 (3H, s), 3.19 (9H, s),
3.86 (3H, s), 5.08 (2H, s), 5.27 (2H, s),
6.83-7.60 (6H, m), 8.35-8.61 (1H, m)

Preparation 10

30 The following compound was prepared according to a similar manner to that of Preparation 9.

35 2-Methyl-8-(2-nitrobenzyloxy)-3-trimethylammonio-methylimidazo[1,2-a]pyridine iodide

mp : >163°C (dec.)

NMR (DMSO-d₆, δ) : Ca 2.4-2.7 (3H, s),

3.11 (9H, s), 4.99 (2H, s), 5.69 (2H, s),
6.80-7.10 (2H, m), 7.63-8.00 (2H, m),
8.06-8.56 (3H, m)

5 Preparation 11

The following compound was prepared according to a similar manner to that of Preparation 2.

2-Amino-3-methoxymethoxypyridine

10 NMR (CDCl₃, δ) : 3.50 (3H, s), 4.40-5.13 (2H, br s), 5.20 (2H, s), 6.46-6.76 (1H, m), 7.20 (1H, dd, J=2Hz, 8Hz), 7.73 (1H, dd, J=2Hz, 5Hz)

Preparation 12

15 A solution of 2-amino-3-methoxymethoxypyridine (7.5 g) and 3-mesyloxy-5-hexyn-2-one (10.18 g) in ethanol (150 ml) was refluxed for 46.5 hours and then evaporated in vacuo. To the residue was added 20% sulfuric acid (75 ml) and the mixture was stirred for
20 5 hours at room temperature. The mixture was made alkaline with sodium bicarbonate and extracted with chloroform. The extract was washed with brine, dried over magnesium sulfate, and evaporated in vacuo. The residue was purified by column chromatography on
25 silica gel (30 g) with chloroform and then a mixture of chloroform and methanol (30:1 to 20:1) as eluents. The eluates were evaporated in vacuo and the residue was recrystallized from a mixture of ethyl acetate and
30 n-hexane to give 8-hydroxy-2-methyl-3-(2-propynyl)-imidazo[1,2-a]pyridine (1.93 g).

mp : 175 to 177°C

NMR (CDCl₃, δ) : 2.03 (1H, t, J=3Hz), 2.45 (3H, s), 3.73 (2H, d, J=3Hz), 6.70-6.90 (2H, m), 7.57-7.76 (1H, m), 11.29 (1H, s)

Preparation 13

A mixture of 2,6-dimethylbenzyl alcohol (8.17 g) and acetic anhydride (8.1 g) was heated at 70°C for 3 hours and evaporated in vacuo. To the residue was added aqueous sodium bicarbonate and extracted with diethyl ether. The extract was washed with water, dried over magnesium sulfate, and evaporated in vacuo to give an oil of 2,6-dimethylbenzyl acetate (10.75 g).

IR (film) : 1720, 1590, 1470, 1380, 1230, 1020 cm^{-1}

NMR (CDCl_3 , δ) : 2.05 (3H, s), 2.37 (6H, s),
5.20 (2H, s), 6.90-7.33 (3H, s)

Preparation 14

Fuming nitric acid (0.52 ml) was added dropwise to a solution of 2,6-dimethylbenzyl acetate (1.78 g) in acetic anhydride (8.9 ml) at 0°C and then stirred for 2.5 hours. After being stirred for an additional 30 minutes at room temperature, the mixture was poured onto crushed ice, neutralized with sodium bicarbonate, and extracted with ethyl acetate. The extract was washed with water and evaporated in vacuo. To the residue were added methanol (24 ml) and 1N sodium hydroxide solution (12 ml) and the mixture was stirred at room temperature for 1 hour and evaporated in vacuo. The residue was washed with water, air-dried, and recrystallized from a mixture of benzene and n-hexane to give 2,6-dimethyl-3-nitrobenzyl alcohol (1.26 g).

mp : 94 to 95°C

IR (Nujol) : 3125, 1580, 1510, 1385, 995 cm^{-1}

NMR (CDCl_3 , δ) : 2.50 (3H, s), 2.55 (3H, s),
4.80 (2H, s), 7.17 (2H, d, $J=8\text{Hz}$),
7.67 (2H, d, $J=8\text{Hz}$)

Preparation 15

2,6-Dimethyl-3-nitrobenzyl chloride was obtained

from 2,6-dimethyl-3-nitrobenzyl alcohol according to a conventional manner.

mp : 54 to 55°C (recrystallized from cyclohexane)

IR (Nujol) : 1595, 1520, 1385, 1270 cm^{-1}

5 NMR (CDCl_3 , δ) : 2.52 (3H, s), 2.57 (3H, s),
4.68 (2H, s), 7.17 (1H, d, $J=8\text{Hz}$),
7.87 (1H, d, $J=8\text{Hz}$)

Example 1

10 A solution of 2-amino-3-(2-methoxybenzyloxy)pyridine
(3.50 g) and 3-tosyloxy-5-hexyn-2-one (4.86 g) in ethanol
(30 ml) was stirred and refluxed for 24 hours and then
evaporated in vacuo. To the residue was added an aqueous
15 solution of sodium bicarbonate and the mixture was
extracted with ethyl acetate. The extract was washed with
water, dried over magnesium sulfate and evaporated in
vacuo. The oily residue was purified by column
chromatography on silica gel (50 g) using chloroform as
an eluent to give a solid, which was recrystallized
20 from a mixture of ethyl acetate and n-hexane to give
8-(2-methoxybenzyloxy)-2-methyl-3-(2-propynyl)imidazo-
[1,2-a]pyridine (1.49 g).

mp : 134 to 136°C

IR (Nujol) : 3365, 3280 cm^{-1}

25 NMR (CDCl_3 , δ) : 2.03 (1H, t, $J=3\text{Hz}$), 2.46 (3H, s),
3.72 (2H, d, $J=3\text{Hz}$), 3.83 (3H, s), 5.36 (2H, s),
6.36-6.73 (2H, m), 6.74-7.02 (2H, m),
7.13-7.41 (1H, m), 7.44-7.59 (1H, m),
7.64 (1H, dd, $J=2\text{Hz}$ and 7Hz)

30 Analysis Calcd. for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_2$:

C 74.49; H 5.92; N 9.14

Found : C 74.85; H 5.97; N 9.15

Example 2

35 The following compounds were prepared according
to a similar manner to that of Example 1.

- (1) 2-Methyl-8-(2-methylthiobenzyloxy)-3-(2-propynyl)-imidazo[1,2-a]pyridine
 mp : 130 to 132°C (recrystallized from a mixture of ethyl acetate and n-hexane)
 5 IR (Nujol) : 3270 cm^{-1}
 NMR (CDCl_3 , δ) : 2.06 (1H, t, J=3Hz), 2.46 (3H, s), 2.49 (3H, s), 3.75 (2H, d, J=3Hz), 5.39 (2H, s), 6.43 (1H, d, J=8Hz), 6.64 (1H, t, J=8Hz), 7.02-7.38 (3H, m), 7.50-7.98 (1H, m),
 10 8.03 (1H, d, J=8Hz)
 Analysis Calcd. for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{OS}$:
 C 70.78; H 5.63; N 8.69
 Found : C 70.96; H 5.63; N 8.60
- 15 (2) 2-Methyl-8-(2-nitrobenzyloxy)-3-(2-propynyl)imidazo[1,2-a]pyridine
 mp : 176.5 to 177.5°C (recrystallized from ethanol)
 IR (Nujol) : 3100, 1545, 1510 cm^{-1}
 NMR ($\text{DMSO}-d_6$, δ) : 2.36 (3H, s), 2.93 (1H, t, J=2Hz), 3.92 (2H, d, J=2Hz), 5.70 (2H, s),
 20 6.63-6.99 (2H, m), 7.43-8.06 (4H, m), 8.15 (1H, dd, J=2Hz and 6Hz)
 Analysis Calcd. for $\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}_3$:
 C 67.28; H 4.70; N 13.08
 25 Found : C 67.63; H 5.18; N 13.03
- (3) 2-Methyl-8-(3-methyl-2-thienylmethoxy)-3-(2-propynyl)-imidazo[1,2-a]pyridine
 mp : 112 to 113°C (recrystallized from a mixture of diethyl ether and n-hexane)
 30 IR (Nujol) : 3300, 1530 cm^{-1}
 NMR (CDCl_3 , δ) : 2.03 (1H, t, J=3Hz), 2.27 (3H, s), 2.43 (3H, s), 3.73 (2H, d, J=3Hz), 5.39 (2H, s), 6.48-6.75 (2H, m), 6.82 (1H, d, J=5Hz), 7.19 (1H, d, J=5Hz), 7.72 (1H, dd, J=1.5Hz and 6Hz)
 35

Analysis Calcd. for $C_{17}H_{16}N_2OS$:

C 68.89; H 5.44; N 9.45

Found : C 68.86; H 5.06; N 9.44

5 (4) 2-Methyl-3-(2-propynyl)-8-(3-pyridylmethoxy)imidazo-
[1,2-a]pyridine
mp : 140 to 142°C (recrystallized from ethyl acetate)
IR (Nujol) : 3600-3200 (broad), 3310, 1585,
1540 cm^{-1}

10 NMR ($CDCl_3$, δ) : 1.96-2.16 (1H, m), 2.46 (3H, s),
3.74 (2H, d, $J=3Hz$), 5.33 (2H, s),
6.34-6.81 (2H, m), 7.11-7.40 (1H, m),
7.60-8.0 (2H, m), 8.52 (1H, dd, $J=2Hz$ and $5Hz$),
8.68 (1H, d, $J=2Hz$)

15 Analysis Calcd. for $C_{17}H_{15}N_3O$:

C 73.63; H 5.45; N 15.15

Found : C 73.35; H 5.40; N 14.73

20 (5) 8-(2-Mesylbenzyloxy)-3-(2-propynyl)-2-
methylimidazo[1,2-a]pyridine
mp : 179 to 180°C

Example 3

25 A solution of m-chloroperbenzoic acid (4.53 g)
in methylene chloride (56 ml) was added dropwise to a
solution of 2-methyl-8-(2-methylthiobenzyloxy)-3-(2-
propynyl)imidazo[1,2-a]pyridine (2.4 g) in methylene
chloride (72 ml) with ice-cooling and stirring over a
period of 10 minutes. After being stirred for 93 hours
30 at ambient temperature, the solution was washed
successively with aqueous sodium bicarbonate, water,
and saturated sodium chloride aqueous solution, dried
over magnesium sulfate, and evaporated in vacuo.
The residue was purified by column chromatography on
35 silica gel (60 g) with chloroform as an eluent to

afford a solid, which was recrystallized from a mixture of ethanol and tetrahydrofuran to give 8-(2-mesybenzyloxy)-2-methyl-3-(2-propynyl)imidazo[1,2-a]-pyridine (0.53 g).

5 mp : 179 to 180°C
 IR (Nujol) : 3180 cm^{-1}
 NMR (CDCl_3 , δ) : 2.08 (1H, t, $J=3\text{Hz}$),
 2.40 (3H, s), 3.27 (3H, s), 3.75 (2H, d,
 $J=3\text{Hz}$), 5.67 (2H, s), 6.56-6.87 (2H, m),
10 7.41-7.83 (4H, m), 8.03-8.20 (1H, m)
 Analysis Calcd. for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_3\text{S}$:
 C 64.39; H 5.12; N 7.90
 Found : C 64.30; H 4.92; N 7.78

15 Example 4

 Potassium carbonate (0.52 g) was added to a solution of 8-hydroxy-2-methyl-3-(2-propynyl)imidazo[1,2-a]-pyridine (0.5 g) and 4-chloromethyl-3-methylpyridine (0.53 g) in N,N-dimethylformamide (10 ml). The mixture
20 was stirred under a nitrogen atmosphere for 5 hours at room temperature and then poured into water. The resulting precipitates were collected by filtration and recrystallized from ethyl acetate to give 2-methyl-8-(3-methyl-4-pyridylmethoxy)-3-(2-propynyl)imidazo[1,2-a]-
25 pyridine (0.58 g).

 mp : 156 to 157°C
 NMR ($\text{DMSO}-d_6$, δ) : 2.36 (6H, s), 2.95 (1H, t,
 $J=3\text{Hz}$), 3.93 (2H, d, $J=3\text{Hz}$), 5.37 (2H, s),
 6.70-6.90 (2H, m), 7.49 (1H, d, $J=5\text{Hz}$),
30 7.85-8.03 (1H, m), 8.39-8.53 (2H, m)
 Analysis Calcd. for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}$:
 C 74.21; H 5.88; N 14.42
 Found : C 74.53; H 6.02; N 14.47

35

Example 5

The following compounds were prepared according to a similar manner to that of Example 4.

- 5 (1) 2-Methyl-8-(2-methyl-3-pyridylmethoxy)-3-(2-propynyl)imidazo[1,2-a]pyridine
mp : 167 to 169°C (recrystallized from ethyl acetate)
NMR (CDCl₃, δ) : 2.06 (1H, t, J=3Hz), 2.46 (3H, s),
10 2.63 (3H, s), 3.78 (2H, d, J=3Hz), 5.31 (2H, s),
6.36-6.86 (2H, m), 6.98-7.33 (1H, m),
7.65-7.92 (2H, m), 8.43 (1H, dd, J=2Hz, 5Hz)
- 15 (2) 2-Methyl-8-(3-methyl-2-pyridylmethoxy)-3-(2-propynyl)-imidazo[1,2-a]pyridine
mp : 133 to 134°C (recrystallized from a mixture of ethyl acetate and diisopropyl ether)
NMR (CDCl₃, δ) : 2.05 (1H, t, J=3Hz), 2.45 (3H, s),
20 2.52 (3H, s), 3.75 (2H, d, J=3Hz), 5.46 (2H, s), 6.63-6.86 (2H, m), 7.03-7.80 (3H, m), 8.35-8.56 (1H, m)
Analysis Calcd. for C₁₈H₁₇N₃O :
C 74.21; H 5.88; N 14.42
25 Found : C 74.24; H 5.80; N 14.49
- 30 (3) 8-(2-Acetamidothiazol-4-ylmethoxy)-2-methyl-3-(2-propynyl)imidazo[1,2-a]pyridine
mp : 176 to 178°C (recrystallized from a mixture of ethyl acetate and n-hexane)
NMR (CDCl₃, δ) : 2.06 (1H, t, J=3Hz), 2.20 (3H, s), 2.43 (3H, s), 3.75 (2H, d, J=2Hz),
5.20 (2H, s), 6.43-6.86 (2H, m), 6.95 (1H, s),
7.72 (1H, dd, J=2Hz, 6Hz), 11.0-11.60 (1H, br s)
35

(4) 8-(3,5-Dimethyl-4-methoxy-2-pyridylmethoxy)-2-methyl-3-(2-propynyl)imidazo[1,2-a]pyridine

mp : 158 to 159°C (recrystallized from a mixture of ethanol and diisopropyl ether)

5 IR (Nujol) : 3225, 1565, 1545, 1405, 1290 cm^{-1}

NMR (CDCl_3 , δ) : 2.05 (1H, t, J=3Hz), 2.27 (3H, s), 2.42 (3H, s), 2.43 (3H, s), 3.76 (2H, m), 3.77 (3H, s), 5.40 (2H, s), 6.53-6.90 (2H, m), 7.67 (1H, dd, J=2Hz, 6Hz), 8.23 (1H, s)

10

Example 6

To a solution of sodium hydride (63.6% in mineral oil dispersion, 0.282 g) in 2-propynyl alcohol (14 ml) was added 8-(2-methoxybenzyloxy)-2-methyl-3-trimethyl-ammoniomethylimidazo[1,2-a]pyridine iodide (3.43 g) and the mixture was heated at 90-95°C with stirring for 1 hour. After being cooled, the mixture was poured into ice-water and the resulting precipitate was collected by filtration and dissolved in methylene chloride. The solution was treated successively with silica gel (1 g) and activated charcoal and evaporated in vacuo. The crystalline residue was recrystallized from a mixture of ethyl acetate and n-hexane to give 8-(2-methoxybenzyloxy)-2-methyl-3-(2-propynyloxymethyl)-imidazo[1,2-a]pyridine (1.85 g).

20

25

mp : 107 to 108°C

NMR (CDCl_3 , δ) : 2.40-2.60 (1H, m), 2.50 (3H, s), 3.85 (3H, s), 4.06 (2H, d, J=2Hz), 4.86 (2H, s), 5.36 (2H, s), 6.40-6.73 (2H, m), 6.91 (2H, t, J=8Hz), 7.27 (1H, m), 7.50 (1H, b.d, J=8Hz), 7.72 (1H, dd, J=15 Hz, 6Hz)

30

Example 7

35 The following compound was prepared according to a similar manner to that of Example 6.

2-Methyl-8-(2-nitrobenzyloxy)-3-(2-propynyloxymethyl)-
imidazo[1,2-a]pyridine

mp : 145 to 146°C (recrystallized from a mixture
or ethyl acetate and n-hexane)

5 NMR (CDCl₃, δ) : 2.53 (3H, s), 2.43-2.70 (1H, m),
4.10 (2H, d, J=2Hz), 4.90 (2H, s), 5.73
(2H, s), 6.33-6.83 (2H, m), 7.23-8.06 (4H, m),
8.16 (1H, dd, J=2Hz, 8Hz)

10 Example 8

The following compounds were prepared according to
a similar manner to that of Example 4.

15 (1) 8-(2,6-Dimethyl-3-nitrobenzyloxy)-2-methyl-3-
(2-propynyl)imidazo[1,2-a]pyridine

mp : 147 to 149°C (recrystallized from a mixture of
ethyl acetate and n-hexane)

IR (Nujol) : 3290, 1540, 1505, 1410, 1345, 1275,
1080 cm⁻¹

20 NMR (CDCl₃, δ) : 2.30 (1H, t, J=3Hz), 2.43 (3H, s),
2.50 (3H, s), 2.53 (3H, s), 3.78 (2H, d,
J=3Hz), 5.30 (2H, s), 6.68 (1H, dd, J=2Hz,
7.5Hz), 6.80 (1H, t, J=7.5Hz), 7.20 (1H, d,
J=8Hz), 7.73 (1H, d, J=8Hz), 7.83 (1H, dd,
25 J=2Hz, 7.5Hz)

Analysis Calcd. for C₂₀H₁₉N₃O₃ :

C 68.75; H 5.48; N 12.03

Found : C 69.05; H 5.32; N 11.73

30 (2) 2-Methyl-8-(2-methyl-6-nitrobenzyloxy)-3-(2-propynyl)-
imidazo[1,2-a]pyridine

mp : 177 to 178°C (recrystallized from ethyl acetate)

IR (Nujol) : 1540, 1510, 1280 cm⁻¹

35 NMR (CDCl₃, δ) : 2.03 (1H, t, J=3Hz), 2.40 (3H, s),
2.53 (3H, s), 3.72 (2H, d, J=3Hz), 5.43 (2H, s),
6.45-6.77 (2H, m), 7.25-7.46 (2H, m),
7.53-7.77 (2H, m)

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- (3) 2-Methyl-8-(4-methyl-3-pyridylmethoxy)-3-(2-propynyl)imidazo[1,2-a]pyridine
mp : 127 to 128°C (recrystallized from ethyl acetate)

5 IR (Nujol) : 3240, 1600, 1565, 1540, 1495, 1285 cm^{-1}

10 NMR (CDCl_3 , δ) : 2.04 (1H, t, J=3Hz), 2.43 (6H, s), 3.73 (2H, d, J=3Hz), 5.26 (2H, s), 6.47 (1H, dd, J=2Hz, 7.5Hz), 6.50-6.74 (1H, m), 7.05 (1H, d, J=5Hz), 7.65 (1H, dd, J=2Hz, 6Hz), 8.35 (1H, d, J=5Hz), 8.50 (1H, s)

- (4) 2-Methyl-8-(2-methyl-3-nitrobenzyloxy)-3-(2-propynyl)imidazo[1,2-a]pyridine

15 mp : 191 to 192°C (recrystallized from methanol)
IR (Nujol) : 3170, 1540, 1505, 1345, 1280, 1095 cm^{-1}
NMR (CDCl_3 , δ) : 2.04 (1H, t, J=3Hz), 2.45 (3H, s), 2.50 (3H, s), 3.75 (2H, d, J=3Hz), 5.33 (2H, s), 6.42 (1H, dd, J=2Hz, 7.5Hz), 6.65 (1H, t, J=7.5Hz), 7.10-7.35 (1H, m), 7.53-7.77 (3H, m)

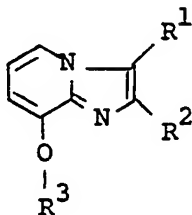
- (5) 2-Methyl-8-(2-methyl-5-nitrobenzyloxy)-3-(2-propynyl)imidazo[1,2-a]pyridine

25 mp : 203 to 205°C (recrystallized from methanol)
IR (Nujol) : 3270, 1540, 1345, 1285 cm^{-1}
NMR ($\text{DMSO}-d_6$, δ) : 2.33 (3H, s), 2.48 (3H, s), 2.93 (1H, t, J=3Hz), 3.90 (2H, d, J=3Hz), 5.38 (2H, s), 6.70-6.93 (2H, m), 7.48 (1H, d, J=8Hz), 7.80-7.93 (1H, m), 8.07 (1H, dd, J=2Hz, 8Hz), 8.31 (1H, d, J=2Hz)

35

What we claim is :

1. An imidazopyridine compound of the formula :



wherein R^1 is lower alkynyl or lower alkynyloxy-(lower)alkyl,
 R^2 is lower alkyl, and
 R^3 is ar(lower)alkyl having lower alkoxy,
 15 lower alkylthio, nitro or lower alkanesulfonyl, ar(lower)alkyl having nitro and one or two additional substituent(s) selected from nitro and lower alkyl, or heterocyclic(lower)alkyl which may
 20 have suitable substituent(s),
 and a pharmaceutically acceptable salt thereof.

2. A compound of claim 1, wherein
 R^3 is phenyl(lower)alkyl having lower alkoxy,
 25 lower alkylthio, nitro or lower alkanesulfonyl.
3. A compound of claim 2, wherein
 R^3 is benzyl having methoxy, methylthio, nitro or mesyl.
 30
4. A compound of claim 3, which is selceted from a group consisting of :
 8-(2-methoxybenzyloxy)-2-methyl-3-(2-propynyl)-imidazo[1,2-a]pyridine,
 35 2-methyl-8-(2-methylthiobenzyloxy)-3-(2-propynyl)-imidazo[1,2-a]pyridine,

- 2-methyl-8-(2-nitrobenzyloxy)-3-(2-propynyl)imidazo-
[1,2-a]pyridine,
8-(2-mesybenzyloxy)-2-methyl-3-(2-propynyl)imidazo-
[1,2-a]pyridine,
5 8-(2-methoxybenzyloxy)-2-methyl-3-(2-propynyloxy-
methyl)imidazo[1,2-a]pyridine, and
2-methyl-8-(2-nitrobenzyloxy)-3-(2-propynyloxy-
methyl)imidazo[1,2-a]pyridine
- 10 5. A compound of claim 4, which is
8-(2-methoxybenzyloxy)-2-methyl-3-(2-propynyl)-
imidazo[1,2-a]pyridine.
- 15 6. A compound of claim 4, which is
8-(2-methoxybenzyloxy)-2-methyl-3-(2-propynyloxy-
methyl)imidazo[1,2-a]pyridine.
- 20 7. A compound of claim 1, wherein
 R^3 is phenyl(lower)alkyl having nitro and one or
two additional substituent(s) selected from
nitro and lower alkyl.
- 25 8. A compound of claim 7, wherein
 R^3 is benzyl having nitro and one or two additional
substituent(s) selected from nitro and methyl.
- 30 9. A compound of claim 8, which is selected from
a group consisting of :
8-(2,6-dimethyl-3-nitrobenzyloxy)-2-methyl-3-(2-
propynyl)imidazo[1,2-a]pyridine,
2-methyl-8-(2-methyl-6-nitrobenzyloxy)-3-(2-
propynyl)imidazo[1,2-a]pyridine,
2-methyl-8-(2-methyl-3-nitrobenzyloxy)-3-(2-
propynyl)imidazo[1,2-a]pyridine, and
35 2-methyl-8-(2-methyl-5-nitrobenzyloxy)-3-(2-
propynyl)imidazo[1,2-a]pyridine.

10. A compound of claim 1, wherein
R³ is 3 to 7 membered heteromonocyclic(lower)alkyl
which may have lower alkyl, lower alkoxy or
acylamino.

5

11. A compound of claim 10, wherein
R³ is thienyl having methyl,
thiazolyl having acetamido or
pyridyl which may have methyl or methoxy.

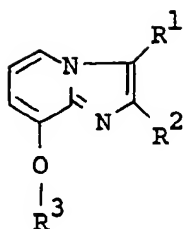
10

12. A compound of claim 11, which is selected from a
group consisting of :
2-methyl-8-(3-methyl-2-thienylmethoxy)-3-(2-
propynyl)imidazo[1,2-a]pyridine,
15 2-methyl-3-(2-propynyl)-8-(3-pyridylmethoxy)imidazo-
[1,2-a]pyridine,
2-methyl-8-(3-methyl-4-pyridylmethoxy)-3-(2-propynyl)-
imidazo[1,2-a]pyridine,
2-methyl-8-(2-methyl-3-pyridylmethoxy)-3-(2-propynyl)-
20 imidazo[1,2-a]pyridine,
2-methyl-8-(3-methyl-2-pyridylmethoxy)-3-(2-propynyl)-
imidazo[1,2-a]pyridine,
8-(2-acetamidothiazol-4-ylmethoxy)-2-methyl-3-(2-
propynyl)imidazo[1,2-a]pyridine,
25 8-(3,5-dimethyl-4-methoxy-2-pyridylmethoxy)-2-
methyl-3-(2-propynyl)imidazo[1,2-a]pyridine,
and
2-methyl-8-(4-methyl-3-pyridylmethoxy)-3-(2-propynyl)-
imidazo[1,2-a]pyridine.

30

13. A process for preparing imidazopyridine compounds
of the formula :

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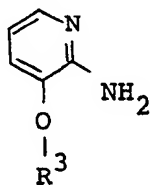
wherein R^1 is lower alkynyl or lower alkynyloxy(lower)alkyl,
 R^2 is lower alkyl, and
 R^3 is ar(lower)alkyl having lower alkoxy,
 10 lower alkylthio, nitro or lower
 alkanesulfonyl, ar(lower)alkyl having
 nitro and one or two additional substituent(s)
 selected from nitro and lower alkyl,
 15 or heterocyclic(lower)alkyl which may
 have suitable substituent(s)

or a salt thereof,

which comprises

(1) reacting a compound of the formula :

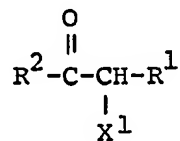
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wherein R^3 is as defined above,
 or a salt thereof,
 with a compound of the formula :

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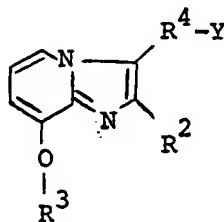
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wherein R^1 and R^2 are each as defined above,
and
 X^1 is an acid residue,
or

5

(2) reacting a compound of the formula :

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wherein R^2 and R^3 are each as defined above,
 R^4 is lower alkylene, and
 Y is a leaving group,
or a salt thereof,
with a compound of the formula :

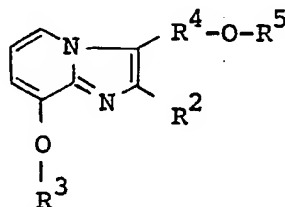
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wherein R^5 is lower alkynyl,
or a salt thereof,
to give a compound of the formula :

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wherein R^2 , R^3 , R^4 and R^5 are each as defined
above,
or a salt thereof,
or

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(3) subjecting a compound of the formula :



10 wherein R^1 and R^2 are each as defined above,
and
 R^6 is ar(lower)alkyl which has lower
alkylthio,
or a salt thereof,
to oxidation reaction to give a compound of
15 the formula :



25 wherein R^1 and R^2 are each as defined above,
and
 R^7 is ar(lower)alkyl which has lower
alkanesulfonyl,
or a salt thereof,
or

(4) reacting a compound of the formula :



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wherein R^1 and R^2 are each as defined above,
or a salt thereof,
with a compound of the formula :



wherein R^3 is as defined above and
 X^2 is an acid residue.

- 10 14. A pharmaceutical composition which comprises,
as an active ingredient, a compound of claim 1 or a
pharmaceutically acceptable salt thereof in admixture
with pharmaceutically acceptable carriers.
- 15 15. Use of compounds of claim 1 as a medicament.
16. Use of compounds of claim 1 in treating ulcer.
17. Use of compounds of claim 1 for manufacture of medicament
20 for treating ulcer.

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European Patent
Office

EUROPEAN SEARCH REPORT

0228006
Application number

EP 86 11 7340

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.4)
A	EP-A-0 033 094 (SCHERING CORPORATION) * Claim 1; pages 73-75 * -----	1, 14	C 07 D 471/04 A 61 K 31/435// (C 07 D 471/04 C 07 D 235:00 C 07 D 221:00)
			TECHNICAL FIELDS SEARCHED (Int. Cl.4)
			C 07 D 471/00 A 61 K 31/00
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 23-03-1987	Examiner ALFARO I.
<div>CATEGORY OF CITED DOCUMENTS</div> <div><div>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</div><div>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</div></div>			